another one of the following part-sequence motifs:

$LX_9NX_2YX_2QLLX(D/E)X_{10/11}WGRVG$ (SEQ ID NO: 15),

$AX_3FXKX_4KTXNXWX_5FX_3PXK$ (SEQ ID NO:16),

$QXL(I/L)X_2IX_9MX_{10}PLGKLX_3QIX_6L$ (SEQ ID NO:17),

$FYTXIPHXFGX_3PP$ (SEQ ID NO:18); and

$KX_3LX_2LXDIEXAX_2L$ (SEQ ID NO:19),

in which the X radicals are, independently of one another, any amino acid.

REMARKS

The above amendments to the specification include the insertion of an updated Sequence Listing with current information pertinent to the present application. This information includes the names of the applicants, the serial number of the present application and the application number and filing date of the corresponding international application. This substitute sheets of the Sequence Listing also contain 5 sequences that are found in the body of the specification which were not included in the originally filed Sequence Listing. Additionally, the previous Sequence Listing, which was numbered as pages 48 to 80 of the specification has been replaced with independent pages 48-82 submitted herewith.

Sequence numbers 29 to 33 are found in the original specification on pages 3, 4, 6 and 25 and the origin of these sequences is described on that page, as well. The original specification has also been amended to include the sequence identification numbers where these are appropriate to aid in the identification of the amino acid and nucleic acid sequences to which reference is made.

The amendments to the specification as a whole, and the substitute Sequence Listing in particular, contain no new matter. The computer readable copy of the Sequence Listing attached hereto is identical to the substitute copy of the Sequence Listing here submitted.

The above claims have been amended to introduce sequence listing numbers as required by 37 CFR §1.821(d). No new matter has been introduced by these amendments.

It is believed that by submitting the present amendment and the sequence listing diskette, the application now fully complies with the requirements of 37 CFR §§ 1.821-1.825. Applicants respectfully solicit issuance of the patent.

Please charge any shortage in fees due in connection with the filing of this paper, including Extension of Time fees to Deposit Account No. 11-0345. Please credit any excess fees to such deposit account.

Respectfully submitted,

KEIL & WEINKAUF

Herbert B. Keil
Reg. No. 18,967

1101 Connecticut Ave., N.W.
Washington, D.C. 20036
(202)659-0100

HBK/DCL/kas

Version with markings to show changes in Specification and Claims

IN THE SPECIFICATION

Kindly delete the paragraph beginning on page 3, line 9 and ending on the same page, line 23. Please insert the following paragraph in its place.

We have found that this object is achieved by providing PARP homologs, preferably derived from human and non-human mammals, having an amino acid sequence which has

a) a functional NAD^+ binding domain, i.e. a PARP "signature" sequence having the characteristic GX_3GKG motif (SEQ ID NO:29);
and

b) especially in the N-terminal sequence region, i.e. in the region of the first 200, such as, for example, in the region of the first 100, N-terminal amino acids, no PARP zinc finger sequence motifs of the general formula

$$CX_2CX_mHX_2C$$ (SEQ ID NO:30)

in which

m is an integral value from 28 or 30, and the X radicals are, independently of one another, any amino acid;

and the functional equivalents thereof.

Kindly delete the paragraph beginning on page 4, line 14 and ending on the same page, line 23. Please insert the following paragraph in its place.

The functional NAD^+ binding domain (i.e. catalytic domain) binds the substrate for poly-(ADP-ribose) synthesis. Consistent with known PARPs, the sequence motif $GX^1X^2X^3GKG$ (SEQ ID NO:29), in which G is glycine, K is lysine, and X^1, X^2 and X^3 are, independently of one another, any amino acid, is present in particular. However, as shown, surprisingly, by comparison of the amino acid sequences of the NAD^+ binding

domains of PARP molecules according to the invention with previously disclosed human PARP1, the sequences according to the invention differ markedly from the known sequence for the NAD^+ binding domain.

Kindly delete the paragraph beginning on page 6, line 15 and ending on the same page, line 31. Please insert the following paragraph in its place.

PARP homologs which are particularly preferred according to the invention are the proteins human PARP2, human PARP3, mouse PARP3 and the functional equivalents thereof. The protein referred to as human PARP2 comprises 570 amino acids (cf. SEQ ID NO:2). The protein referred to as human PARP3 possibly exists in two forms. Type 1 comprises 533 amino acids (SEQ ID NO:4) and type 2 comprises 540 amino acids (SEQ ID NO:6). The forms may arise through different initiation of translation. The protein referred to as mouse PARP3 exists in two forms which differ from one another by a deletion of 5 amino acids (15 bp). Type 1 comprises 533 amino acids (SEQ ID NO: 8) and type 2 comprises 528 amino acids (SEQ ID NO:10). The PARP-homologs of the present invention differ in their sequences significantly over said PARP protein of Arabidopsis thaliana (see above). For example, PARP2 and PARP3 do not comprise the plant PARP specific peptide sequence AAVLDQWIPD (SEQ ID NO:31), corresponding to amino acid residues 143 to 152 of the Arabidopsis protein.

Kindly delete the paragraph beginning on page 25, line 29 and ending on the same page, line 35. Please insert the following paragraph in its place.

Variant human PARP2a: Deletion of base pairs 766 to 904 (cf. SEQ ID NO:1). This leads to a frame shift with a new stop codon ("TAA" corresponding to nucleotides 922 to 924 in SEQ ID NO:1).

Variant human PARP2b: Insertion of

5'- gta tgc cag gaa ggt cat ggg cca gca aaa ggg tct ctg -3' (SEQ ID NO:32) after nucleotide 204 (SEQ ID NO:1). This extends the amino acid sequence by the insertion: GMPGRSWASKRVS (SEQ ID NO:33).

Kindly delete the sequence listing on pages 48 to 80 of the specification and substitute replacement pages 48-82 attached hereto as separate pages.

IN THE CLAIMS

1. (amended) A poly(ADP-ribose) polymerase (PARP) homolog which has an amino acid sequence which has

a) a functional NAD^+ binding domain

and

b) no zinc finger sequence motif of the general formula

$$CX_2CX_mHX_2C$$ (SEQ ID NO:30)

in which

m is an integral value from 28 or 30, and the X radicals are, independently of one another, any amino acid;

and the functional equivalents thereof.

2. (amended) A PARP homolog as claimed in claim 1, wherein the functional NAD^+ binding domain comprises one of the following general sequence motifs:

$Px_n(S/T)GX_3GKGIYFA$ (SEQ ID NO:11),

$(S/T)XGLR(I/V)XPX_n(S/T)GX_3GKGIYFA$ (SEQ ID NO:12) or

$LLWHG(S/T)X_7IL(S/T)XGLR(I/V)XPX_n(S/T)GX_3GKGIYFAX_3SKSAXY$ (SEQ ID NO:13)

in which

n is an integral value from 1 to 5, and the X radicals are, independently of one another, any amino acid.

3. (amended) A PARP homolog as claimed in claim 1, comprising at least

another one of the following part-sequence motifs:

$LX_9NX_2YX_2QLLX(D/E)X_{10/11}WGRVG$ (SEQ ID NO: 15),

$AX_3FXKX_4KTXNXWX_5FX_3PXK$ (SEQ ID NO:16),

$QXL(I/L)X_2IX_9MX_{10}PLGKLX_3QIX_6L$ (SEQ ID NO:17),

$FYTXIPHXFGX_3PP$ (SEQ ID NO:18); and

$KX_3LX_2LXDIEXAX_2L$ (SEQ ID NO:19),

in which the X radicals are, independently of one another, any amino acid.